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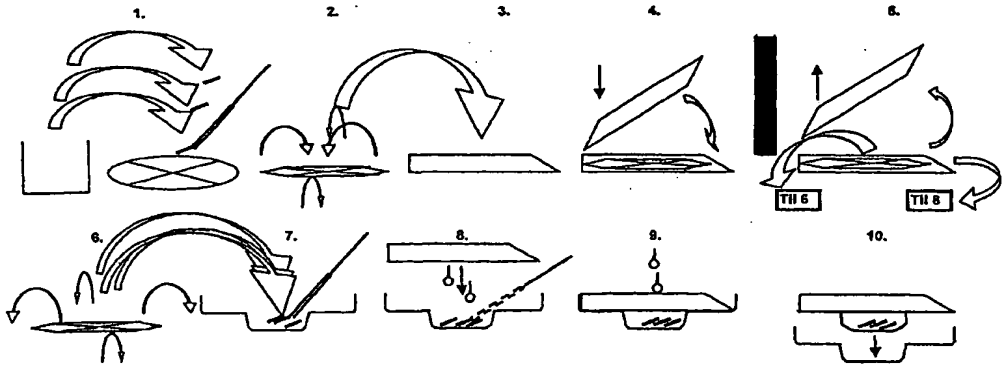

(57) Abstract

The biopsy cassette assembly comprises a cassette (3), a first lid (1) that accompanies the assembly as a seperate unit or is attached to a second lid (2) that is detachably attached to the cassette (3) by a through hole (7) in the cassette (3). A partly perforated detachable basket (5) is attached to the underside of the cassette (3), in which basket (5) a tissue sample should be held after the biopsy has been performed, and the basket (5) extends down into a container (6) that is filled with a tissue fixation medium such as formalin, and which is designed to be detachably attached to the underside of the cassette (3). A method for biopsy preparation by use of a biopsy cassette assembly, in which a solid gel–biopsy–button is formed in a basket (5) detachably attached to the underside of a cassette (3) by filling heated gel in the basket (5) and then cooling it. A cassette–gel–tissue paraffin aggregate is formed by filling heated paraffin in the basket (5) through a perforated first lid (1) attached to the top of the cassette (3) by means of a through hole (7) in the cassette.

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Biopsy cassette assembly and method for biopsy preparation by use of the biopsy cassette assembly

The present invention regards a biopsy cassette assembly as stated in the introduction to Claim 1, as well as a method for biopsy preparation by use of the biopsy cassette assembly, as stated in the introduction to Claim 8.

The term biopsy is taken to mean small tissue preparations that are taken with a pair of biopsy forceps, a biopsy needle or another sharp implement, and which have become a more important area within medicine to allow a diagnosis to be made at the earliest possible stage. These tissue samples have become smaller and greater in numbers, as the techniques for taking biopsies have become more advanced (biopsy needles and fibre-optic biopsy technology).

As a result of biopsies having become a necessity within medicine, problems with the quality of biopsies have become less tolerated by patients and clinicians, and the biopsy laboratories are subjected to stricter formal quality requirements, not least due to more extensive use of DNA testing, in which contamination of samples is a serious problem. Moreover, the extensive use of biopsies calls for simple and inexpensive handling of the samples.

Today's methods of handling, chemical processing and embedding biopsies have not been developed sufficiently to be able to satisfy the above.

Some problems that arise when using today's methods:

- Insufficient tissue for diagnosis, no tissue in the glass received by the laboratory. It is estimated that this problem arises in 1.37 % of all cases in a reasonably large Scandinavian university hospital laboratory, while the figure for a small American university hospital laboratory is 1.72 %. The reasons may be: The surgeon did not get enough tissue, the wrong collection container was sent for analysis, tissue is left behind on the biopsy implement, tissue left on the grossing room forceps, tissue has fallen out of the cassette tissue wrapping, which often happens, as it is normal for

tissue to be found in the chemical processing mechanism, tissue remains in the cassette tissue wrapping, tissue left on the embedding forceps.

Attrition of tissue during handling by the pathology laboratory is an uncontrolled quality problem, as a result of some pieces never appearing on themicroscopic glass slide, which is not registered due to diagnostic tissue being present in the section.

The above occurs as a result of imperfections in today's biopsy handling system, and one of the objects of the present invention is to prevent this.

- A further problem is cross contamination between biopsies, particularly in molecular pathology, where DNA from multiple patients can often be found in a single biopsy block. Q-probes in 275 laboratories thus showed microscopic contaminants in blocks in 3.7 % of the cases. This can happen as a result of forceps being used in the grossing room or the embedding bench.

Cross contamination between tissue samples may lead to erroneous diagnosis and render a DNA analysis meaningless.

The object of the present invention is to reduce this problem by not carrying out any tissue transfers.

- There will often be a greater number of biopsy pieces present on the microscopic glass slide than that given by the surgeon, as a result of tissue being shaken in the biopsycollection container, or fragmentation may occur as a result of damages caused by laboratory forceps.

The object of the present invention is to reduce the biopsy fragmentation through protecting the tissue against shaking and preventing tissue transfer.

- A further disadvantage of previously known methods is erroneous labelling or no labelling of the samples. A Q-probe survey in 417 laboratories revealed erroneous labelling from the operating room in 0.58 % of the cases. This will disrupt the flow of the laboratory work and at worst lead to the patient not receiving a diagnosis or the biopsy procedure having to be repeated.

In 1996, 0.34% erroneous labelling was discovered in a Scandinavian university hospital laboratory, while in 1997 0.27% erroneous labelling was discovered in the same laboratory. These are cases that were discovered, however there is no guarantee that there were more cases that were not discovered, but which led to erroneous diagnosis.

The object of the present invention is to avoid the above, as the biopsy collection container is coded from the factory, by means of which the work intensive operation of labelling and the therewith associated potential of erroneous labelling is avoided.

- By using existing methods, the actual labour cost associated with handling and feeding of biopsy from the tissue container to a finished embedded block is 5 % of the total labour cost in a pathology laboratory.

By using the present invention, the intention is to reduce the costs by 1/2-3/4 of the work.

- Moreover, the task of transferring biopsies from a container to cassettes and dictating a biopsy description is monotonous, and this work may advantageously be performed by a machine.

However, previously known methods do not provide this possibility, and an object of the present invention is therefore to make possible a cassette that may be chemically processed and embedded automatically in a machine with one manual step only.

In this connection it should be mentioned that a cassette is known from US patent no. 5 424 040, the inventor of which incidentally is the same as for the present application, in which a cassette device has a convex membrane that is (a bubble of) a perforated membrane attached at the lower opening of the cassette. I.e., the entire "basket" is perforated. The inventor has found this known solution to be too fragile for the trauma, to which cassettes are subjected during chemical feeding (several cassettes in a pile in the feeding chamber). For this reason, the inventor has developed a new unit in which the convex membrane is replaced by a basket where only the bottom, flat, horizontal section of the rigid plastic basket is partly open and covered by a flat, perforated

membrane. A membrane bubble (the convex membrane) can not protect the integrity of the biopsy, as the cassette assemblies, when in the feeding chamber, are subjected to physical traumas that may lead to a membrane puncturing and tissue leaking out, which is something the present invention intend to secure against, so that no tissue is lost from the cassette.

The above is provided by means of a cassette of the type mentioned at the beginning, the characteristics of which appear from Claim 1, together with a method for biopsy preparation by use of a biopsy cassette assembly, the characteristics of which method appear from Claim 8. Further characteristics of the invention appear from the remaining, dependent claims.

In the following, the invention will be described in greater detail with reference to the drawings, in which:

Fig. 1 shows today's biopsy handling;
Fig. 2 shows the biopsy cassette according to the invention; and
Fig. 3 shows the steps in the present invention.

In the following, the steps of a commonly used method today will be described with reference to figure 1, in order to throw light on the simplification that is achieved by the present invention.

At step 1, the biopsies are taken using a pair of forceps, from a glass into which the samples were placed by the surgeon performing the biopsy, and placed onto a filter paper, which at step 2 is folded around the biopsy and put into a cassette, i.e. a flat, open box (shown as a surface in the figures) (step 3), and at step 4 a lid is placed over the cassette that contains the folded-up paper with the biopsy.

Over night, chemical processing is carried out in an automatic machine between steps 4 and 5.

At step 5, the lid is removed, and at step 6 the filter paper is removed from the cassette, the biopsies are uncovered by folding out the paper, and the biopsy is lifted with a pair of forceps and put into a dish, step 7.

At step 8, heated paraffin in poured into the mould containing the biopsy, and said cassette is placed on the mould. At step 9, more paraffin is applied to said cassette, the bottom of which is perforated. At step 10, the cassette with the attached paraffin and the biopsy is taken out of the mould, and a section is made for microscopy.

As mentioned previously, this process includes many complicated steps that are fraught with problems and disadvantages as indicated earlier.

The above problems and the number of steps are reduced by the present invention, with the aid of a biopsy cassette assembly as shown in figure 2.

The assembly comprises a first lid 1 preferably made of xylene resistant, hard, clear plastic, which is perforated, the apertures preferably having a diameter in the order of 1 mm. The lid 1 may be screwed down into a second lid 2 made of e.g. ordinary semi-rigid, clear plastic, or it may come with the assembly as part of the equipment for the biopsy examination.

This second lid 2 is screwed down into a cassette 3 made of e.g. xylene resistant, hard, plastic with a through hole 7, into which hole 7 the second lid 2 has been screwed down, and into which hole 7 the first lid 1 may be screwed down or pressed down after the second lid 2 has been removed at the laboratory. Markings, for instance bar codes, may be provided at one end of the cassette 3.

To the underside of the cassette 3 is attached a partly perforated detachable basket 5 made of coloured, semi-rigid, xylene resistant plastic, in which basket the tissue is to be placed after the biopsy. The bottom of the basket 5 may have a membrane 4 made of an extremely thin, smooth, xylene resistant material (e.g. polycarbonate) with small perforations welded onto it. The basket 5 extends down into a container 6 of e.g. semi-rigid, semi-transparent plastic, which container is filled with formalin or another tissue fixation medium and screwed onto the underside of the cassette 3 or attached to the underside of the cassette 3 through a snap-in action or a force fit.

The following will describe the use of the biopsy cassette with reference to figure 3.

With reference to figure 3 I, a cassette assembly is shown schematically, the way it is delivered from the factory with formalin in the container 6 and possibly a factory applied marking e.g. in the form of bar codes, which marking may be stored electronically in an operating room in order to be available during a biopsy.

During the biopsy, the lid 2 is removed, cf. fig. 3 II, and the biopsy 8 is thrown directly into the container, i.e. into the basket 5. The lid 2 is screwed back onto the cassette 3 and sent from the operating room to the laboratory, where the biopsy pieces are fixed for a few hours/days. The perforations in the bottom of the basket and the basket bottom membrane ensure that the tissue is fixed, cf. fig. 3 III.

Fig.3 IV indicates a first step on a grossing bench, i.e. a laboratory examination table, where the lid 2 and the formalin container 6 are screwed off the cassette 3 and thrown away. The formalin runs down from the tissue chamber (basket 5 and cassette 3), cf. fig. 3 IV. Heated gel is added to the biopsy pieces in the basket in order to form a compact gel-biopsy-button, cf. fig. 3 V. In a few cases it may be necessary to orient the biopsy pieces with a pair of tweezers. The lid 1 with perforations is pressed or screwed down into the opening in the cassette 3, cf. fig. 3 VI. The lid 1 may, when fastened, be flush with the top of the cassette 3, as indicated in the subsequent steps in figure 3, but this is not a requisite characteristic of the invention.

The perforations in the lid 1 are necessary for the subsequent processing, while the gel keeps the pieces together, and the tissue will not be able to disappear during the subsequent processing. This assembly now passes to the so-called chemical processor room, cf. fig. 3 VII, where the assembly undergoes normal chemical processing together with other biopsy samples in a closed retort chamber without opening the lid or any other manipulation.

Thereafter, the cassette containing the biopsy passes to a paraffin embedding bench, cf. fig. 3 VIII, where heated paraffin is disposed in a lid 1 without special visual control or tissue manipulation. The perforations in the lid ensure that the paraffin is embedded with the gel-tissue-button. Fig. 3 IX shows it as a solid unit of hardened cassette-gel-tissue-paraffin aggregate in the space of a few minutes.

After this, the basket 5 is removed from the cassette 3 on the microtome bench, cf. fig. 3 X, this basket up till now having provided protection for the block of tissue. By removing the basket 5, the membrane 4 is also removed. The block of tissue is now ready to be sliced in the microtome. Fig. 3 XI schematically indicates sections through the block of tissue, the cassette giving it a size that allows it to fit in an ordinary microtome.

Steps VI to X are operations that are suited for implementation in a machine that is appropriate to for this purpose.

C l a i m s

1.
A biopsy cassette device comprising an assembly with a first perforated lid (1), a second lid (2) attached to the assembly, and a container (6) filled with a tissue fixation medium, w h e r e i n
the second lid (2) is a solid, non-perforated lid detachably fastened in a through hole (7) in a cassette (3), and where a detachable basket (5) made of a rigid material and with a partly open bottom is attached to the underside of the cassette (3),
a membrane (4) with small perforations is attached to the bottom of the basket (5), and the cassette (3) with its underside abuts the upper edges of the container (6), in such a manner that only the basket (5) extends down into the tissue fixation medium in the container (6), the container being designed to be detachably attached to the underside of the cassette (3).

2.
A biopsy cassette device according to Claim 1, w h e r e i n the second lid (2) is made from clear plastic.

3.
A biopsy cassette device according to Claims 1-2, w h e r e i n the first lid (1) is designed as a loose part of the biopsy cassette device and possibly detachably attached to the second lid (2).

4.
A biopsy cassette device according to Claims 1-3, w h e r e i n the membrane (4) is formed from an extremely thin, smooth, xylene resistant material (e.g. polycarbonate) with small perforations.

5.
A biopsy cassette device according to Claims 1-4, w h e r e i n the biopsy cassette device is manufactured with a code of unique symbols marking, e.g. bar codes at one end of the cassette (3).

6.

A biopsy cassette device according to Claims 1-5, w h e r e i n the biopsy cassette device is pre-equipped with a tissue fixation medium such as formalin in the container (6).

7.

A biopsy cassette device according to Claims 1-6, w h e r e i n the first lid (1) is equipped with thread that co-operates with corresponding thread in the through hole (7) or the first lid (1) is intended to be placed in the through hole (7) of the cassette (3) by force fitting.

8.

A method for biopsy preparation by use of a biopsy cassette device

w h e r e i n

a solid gel-biopsy-button is formed in a solid basket with a partly open bottom and a membrane (4) with small perforations, which basket is detachably attached to the underside of a cassettes (3), by heated gel being filled in the basket (5) and then cooled.

9.

A method for biopsy preparation according to Claim 8, w h e r e i n a cassette-gel-tissue-paraffin block is formed by heated paraffin being filled in the basket (5) through a perforated first lid (1) attached to the top of the cassette (3) by means of a through hole (7) in the cassette (3).

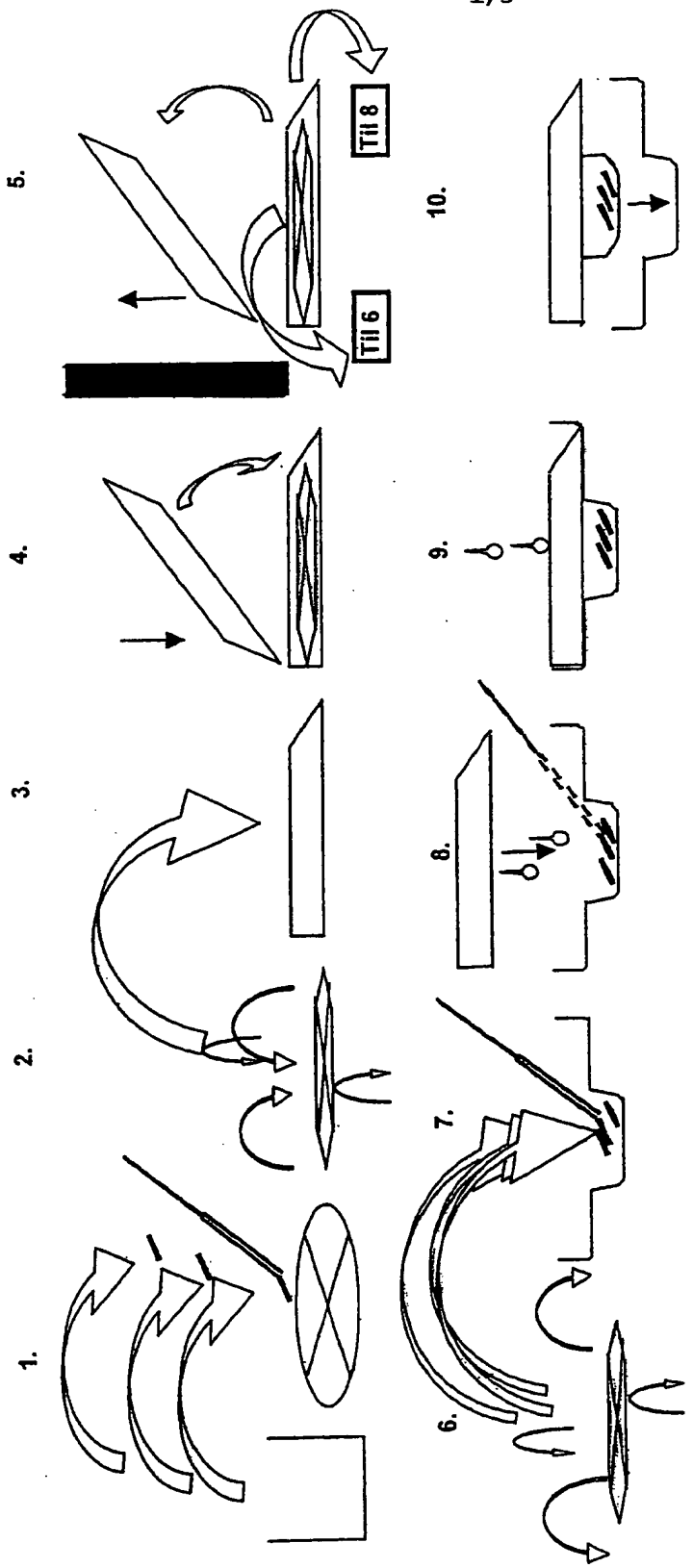

Fig. 1

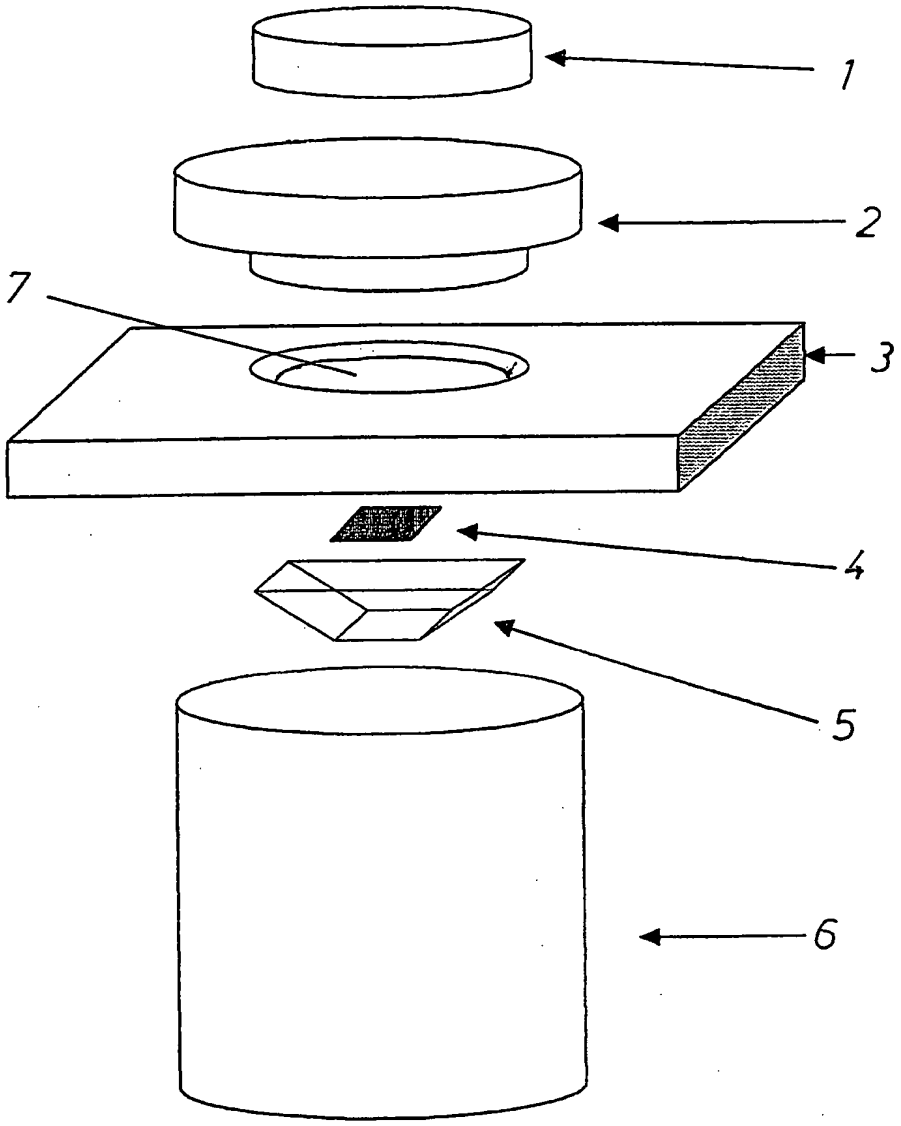

Fig. 2

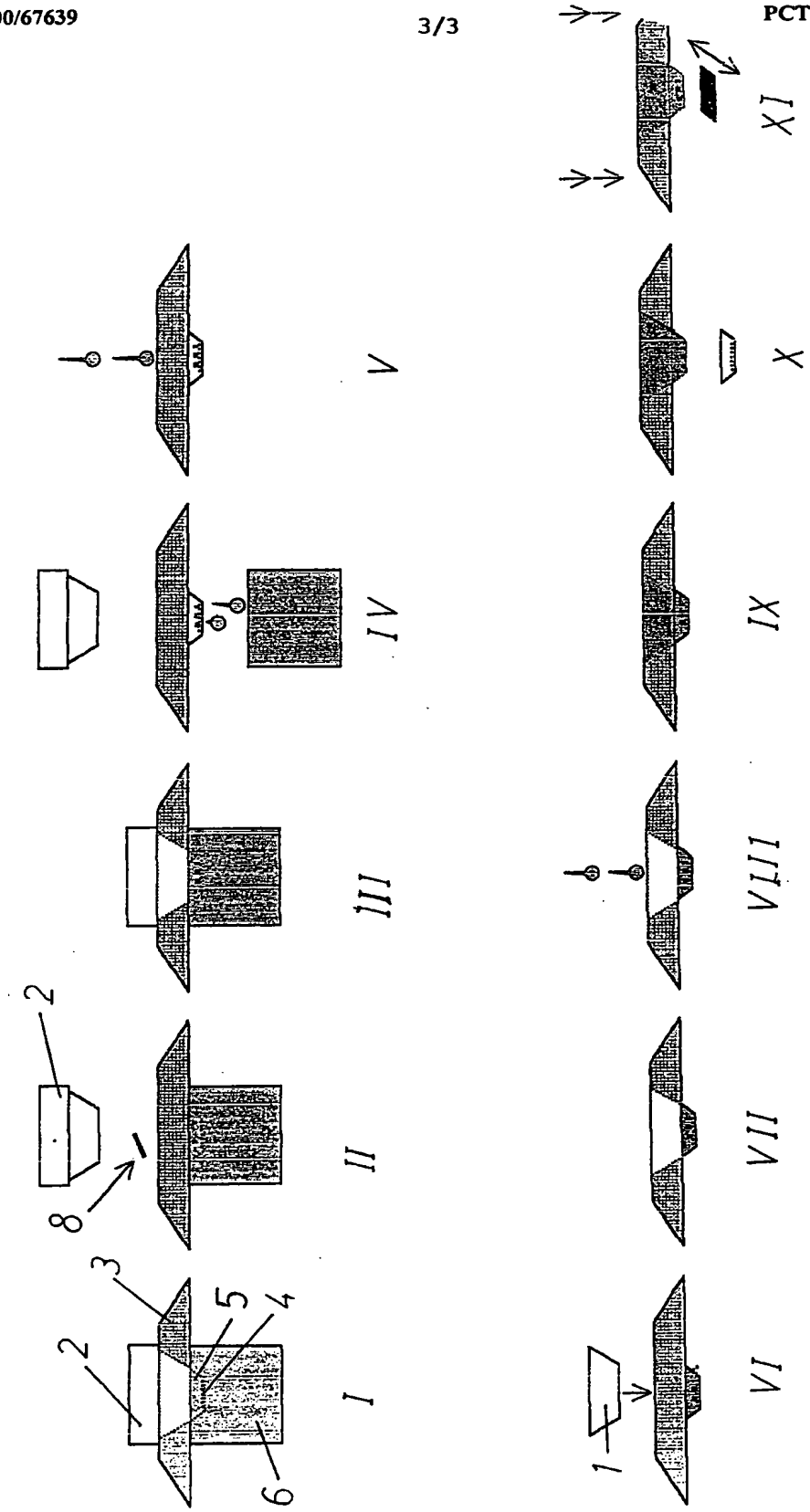

Fig. 3

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NO 00/00138

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61B 10/00
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0807807 A1 (TAKEZAKI, TEIJI), 19 November 1997 (19.11.97), figure 1, abstract ---	1-9
A	US 4801553 A (STEPHEN OWEN ET AL), 31 January 1989 (31.01.89), figures 1-2, abstract ---	1-9
A	US 5061452 A (TADASHI YAMAMOTO ET AL), 29 October 1991 (29.10.91), abstract ---	1-7
A	US 5424040 A (BJORN L. BJORNSSON), 13 June 1995 (13.06.95) --- --------	1-9

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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Information on patent family members

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International application No.
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